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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,182	STOCKERT ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/04/04, 05/20/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-37,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-37 and 40* is/are rejected.

7)☒ Claim(s) *41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *12/20/04* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

It is noted that this Office action replaces the Office action of 07/29/04 to include rejection not previously made.

Accordingly, claims 32-37, 40-41 are being examined.

The following are the remaining rejections.

OBJECTION

Claim 41 appears to be free of pior art but is objected to as being dependent upon a rejected base claims, but would be allowable if rewritten in independent forms, including all of the limitations of the base claim and any intervening claims`.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION, NEW REJECTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 32-37, 40 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 32-37, 40 are drawn to an isolated protein consisting of an immunoreactive portion of a protein encoded by a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:1 (Claim 32). Said protein is processed by a cell to form a peptide which complexes to an MHC molecule and provides a T cell response (Claims 33-37). Said immunoreactive portion of the protein is an amino acid sequence of a tumor rejection antigen (Claim 40).

It is noted that SEQ ID NO:1 is a polynucleotide of 752 nucleotides in length, encoding the NY-ESO-1 protein, which is relatively large and would contain numerous peptide epitopes.

The specification discloses that the peptides of SEQ ID NO:4, 5, and 6 from the NY-ESO-1 polypeptide encoded by SEQ ID NO:1 could elicit a T cell response, wherein SEQ ID NO:4, 5, 6 consists of 11, 9, and 9 amino acids in length, respectively (Example 12, pages 24-25).

The specification discloses several peptides from SEQ ID NO:1 that have HLA binding motifs (Example 13, on pages 25-26).

The specification discloses that melanoma patients contain antibodies in serum to the protein NY-ESO-1, encoded by SEQ ID NO:1 (p.15, first paragraph).

It is noted that although antibodies in serum to the protein NY-ESO-1, encoded by SEQ ID NO:1 is disclosed, the structure of specific peptide epitopes of said antibodies are not disclosed.

In view of a lack of a definition of "immunoreactive portion", and in view of the large size of the protein NY-ESO-1 encoded by SEQ ID NO:1, the claims encompass

numerous different "immunoreactive portions" or peptides derived from the protein encoded by SEQ ID NO:1, wherein said peptides are linear or conformational epitopes of B cells and T cells. Claims 33-37 encompasses numerous peptides derived from the protein encoded by SEQ ID NO:1, that are linear or conformational epitopes of T cells.

It is well known in the art that antigen peptides have to fit into and binds to B cell antigen receptors, which are immunoglobulins on B cell surface for activation of B cells (Stites et al, 1997, Medical Immunology, 9th ed, Appleton & Lange, Stamford, Connecticut, figure 3-9 on page 51, pages 50-51, 118-119). It is also well known in the art that T cell receptors recognize the ligands comprising peptide antigens that are bound to MHC molecules, and that individual T cells respond only to a specific combination of antigen and MHC (Stites et al, supra, page 130). In other words, peptides that are expected to bind to MHC molecules, such as those disclosed in the specification are not necessary ligands of T cell receptors, wherein said ligands provide a T cell response, because T cell receptors have to recognize a specific combination of antigen and MHC, and thus the specification does not provide adequate examples of the claimed T cell epitopes that invokes a T cell response, by providing examples of peptides that are expected to bind to MHC molecules. This is clearly shown by the teaching of Kirkin et al, of record, that only few peptides from melanoma associated antigens have been so far identified as being recognized by specific CTLs, and that some Melan-A/MART-1 peptides although having high affinity for HLA-A2.1 antigen do not induce the generation of melanoma specific CTLs in vitro.

It is further noted that peptide epitopes of B cells and T cells could be linear or conformational to fit into the three dimensional structure of the T cell receptor or into the immunoglobulin binding regions, CDRs, on the surface of B cells, and that each peptide epitope of individual set of B cells or T cells is structurally and/or conformationally different from each other, because of difference in the structure of individual set of B cells or T cell receptors. However, there is no teaching in the specification of whether or not the claimed epitopes are linear or comprise 3-dimensional structures, nor the 3-dimensional structure of the claimed peptide epitopes is disclosed. Herbert et al. (The Dictionary of Immunology, Academic Press, 4th edition, 1995, p.58) define epitopes as the region on an antigen molecule to which antibody or the T cell receptor binds specifically wherein the 3-dimensional structure of the protein molecule may be essential for antibody binding. However, the specification fails to disclose sufficient guidance and objective evidence as to the linear and or three-dimensional conformation of the polypeptide fragments which constitute epitopes recognized by B cell or T cell receptors the claimed invention. Moreover, as evidenced by Greenspan et al., defining epitopes is not as easy as it seems (Nature Biotechnology 7:936-937 (1999). Even when the epitope is defined, in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (page 937, 2nd column).

The specification has not identified which amino acid fragments are critical or essential characteristics of the claimed linear and conformational B and T cell epitopes, other than the linear peptides of SEQ ID NO:4, 5, 6 that elicit CTL response.

Moreover, there is no known common structure of the claimed T cell peptide epitopes of SEQ ID NO: 4,5, or 6, nor is there disclosure of any correlation between common structure of the claimed epitopes and function, i.e. B or T cell response.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials. Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as vertebrate insulin cDNA or mammalian insulin cDNA without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to

define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of the claimed immunoreactive portion, per Lilly by structurally describing a representative number of immunoreactive portions, or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe the immunoreactive portion in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any immunoreactive portion other than SEQ ID NO:4, 5, 6, nor any physical or chemical characteristics of the immunoreactive portion, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses the peptides of SEQ ID NO:4, 5, 6, this does not provide a description of the claimed immunoreactive portions that would satisfy the standard set out in Enzo.

The specification also fails to describe the immunoreactive portions by the test set out in Lilly. The specification describes only the linear peptides of SEQ ID NO:4, 5,6 that induce T cell response. Therefore, it necessarily fails to describe a "representative number" of such species, which includes unknown conformational T and B cell epitopes, in addition to linear B and T cell epitopes of unknown and diverse structure, because each epitope has a unique structure, whether it is linear or conformational. In addition,

the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the immunoreactive portions that is required to practice the claimed invention.

REJECTION UNDER 35 USC 102(b)

Claims 32, 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Morgan DG et al, 1995, J Mass Spectrometry, 30(3): 473-477.

Claims 32 and 40 are drawn to an isolated protein consisting of an immunoreactive portion of a protein encoded by an isolated nucleic acid molecule, consisting of the nucleotide sequence of SEQ ID NO:1. Said immunoreactive portion of the protein is an amino acid sequence of a tumor rejection antigen.

Morgan DG et al teach a tripeptide Gly-Gly-XXX where XXX is Pro.

It is noted that Gly-Gly-Pro is exactly the same as the amino acids 32-34 of the amino acid sequence encoded by SEQ ID NO:1, as shown in the sequence listing on page 36.

It is further noted that SEQ ID NO:1 encodes a tumor rejection antigen as disclosed in the specification.

In addition, it is noted that there is no definition of immunoreactive portion in the specification. Thus the term reads on any reactivity of a portion of the encoded protein with the immune system, wherein this system includes B cells, T cells, Natural killer cells, phagocytes, antigen presenting cells, granulocytes and Platelets etc.. (Roitt I et al,

1993, 3rd ed, Immunology, Mosby, St. Louis, page VI, chapter 2). Any foreign molecule injected into an animal would be recognized by the immune system, and thus be immunoreactive (Stites et al, 1997, supra, page 63).

The peptide taught by the art thus seems to be the same as the claimed immunoreactive protein.

Although the references do not specifically teach an immunoreactive portion of a protein encoded by SEQ ID NO:1, wherein the protein is an amino acid sequence of a tumor rejection antigen, however, the claimed immunoreactive portion appears to be the same as the prior art peptide. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

July 22, 2004

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